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INCREASED RISK OF CERVICAL DYSPLASIA IN LONG TERM SURVIVORS OF ALLOGENEIC STEM CELL TRANSPLANTATION – IMPLICATIONS FOR SCREENING AND HPV VACCINATION

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Cervical, skin and head-neck cancer are most common secondary solid cancers in long-term survivors after allogeneic stem cell transplantation (allo-SCT). Although these cancers are linked to human papillomavirus (HPV) infection, the relationship between HPV and cancers after allo-SCT is not defined. Furthermore, Pap smear screening after SCT is not practiced routinely. We carried out a cross-sectional study of 92 patients receiving allo-SCT for hematological malignancies, enrolled at a minimum of 3 years post-transplantation between 04/2005–06/2007 in an IRB-approved long-term evaluation protocol. Ninety (98%) patients are alive after a median follow-up of 77 months (range 38–167). Evaluation of the 38 female patients (median age at transplant 33, range 9–60 years) included annual gynecological examination. Thirty five received a fractionated total body irradiation (TBI) (12–13.6 Gy) based myeloablative SCT and 3 received a non-TBI non-myeloablative SCT. Acute graft versus host disease (GVHD) (grade II-IV) occurred in 9 (24%) patients and chronic GVHD in 34 (89%), extensive in 10 (26%). Six (16%) patients received immunosuppressive therapy (IST) for chronic GVHD beyond 3 years from SCT. Thirty-five (92%) adult patients had annual cervical smear examinations, 14 (40%) were abnormal. High grade dysplasia was seen in 8 (23%), low grade lesions in 4 (11%) and 2 patients had atypical cells of uncertain significance. Median time to an abnormal smear was 51 months (17–153) and median age of these 12 patients was 42 years (range 19–62). Extensive chronic GVHD requiring prolonged IST was the only factor associated with an increased risk of cervical dysplasia ($p = 0.028$). Our data shows that cervical dysplasia (often high grade) is common after allo-SCT. These patients may be at increased risk of developing invasive cervical cancer. Patients requiring prolonged immunosuppression for chronic GVHD treatment may be especially at risk for all forms of HPV-related malignancy. Aggressive screening and preventive strategies with HPV vaccine appear warranted.

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NATIONAL INSTITUTE OF HEALTH'S RECOMMENDATION FOR ASSESSING LUNG FUNCTION AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION PREDICTS MORTALITY RISK

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Background: The NIH recently published a consensus statement that recommends monitoring FEV1 and DLCO to evaluate changes in lung function after allogeneic hematopoietic cell transplantation (aHCT). Although this recommendation was based upon previous analysis of pre-transplant pulmonary function tests (PFT), their clinical validity and utility have not yet been examined. We conducted an analysis to determine whether FEV1 and DLCO are the most informative measurements for post-transplant lung function change by assessing their relationship with mortality after aHCT. **Methods:** We performed a retrospective review of 1929 patients who underwent aHCT from 1993–2002 and received PFTs within 60–100 days after transplant. Post-transplant FEV1, FVC, TLC, and DLCO were categorized as >/=80, 70–80, 60–70 and < 60% predicted. FEV1/FVC ratio was categorized as >/= 0.7 and < 0.7. Per NIH recommendations lung function score (LFS, range 2–12) was calculated using FEV1 and DLCO. LFS was then categorized from 0–3 (category O = LFS 2; category 1 = LFS 3–5; category 2 = LFS 6–9; category 3 = LFS 10–12). **Results:** Two year all cause mortality after aHCT was 32%. Univariate analysis showed a stepwise increase in mortality with each categorical decrease in FEV1, FVC, TLC, and DLCO. There was no significant relationship between FEV1/FVC ratio and mortality. Mortality increased with increasing LFS (category 1 hazard ratio [HR], 1.50; category 2 HR, 2.86; category 3 HR, 5.64; $p < 0.001$; c-statistic 0.6). The LFS appeared to have a stronger association with mortality than did any individual lung function parameter. However, the LFS was not uniformly distributed with a significantly lower number of patients in LFS categories 2 and 3 (mean LFS score 3.3). **Summary:** These results suggest that decreased lung function by day 100 following aHCT is a risk factor for mortality. An elevated LFS is associated with an increased risk of mortality. The LFS may serve as a mechanism to grade severity of decreased lung function in future clinical trials. However, the scoring system may need to be altered to improve discrimination as it is currently weighted towards patients with normal to near normal lung function. **Abbreviations:** FEV1=Forced expiratory volume in 1 sec, FVC=Forced vital capacity, TLC=Total lung capacity, DLCO=Diffusion capacity of carbon monoxide.

Two year mortality as a function of post-transplant lung function parameters and lung function score categories

Lung function parameters	Died (%)	HR (95% CI)	p-value
FEV1 (%) (n = 1929)			
>80	388/1397 (28)	Referent	
70–80	112/310 (36)	1.39 (1.13–1.72)	0.002
60–70	66/144 (46)	1.96 (1.51–2.55)	<0.001
<60	56/78 (72)	3.84 (2.90–5.09)	<0.001
FVC (%) (n = 1929)			
>80	429/1545 (28)	Referent	
70–80	103/236 (44)	1.81 (1.46–2.25)	<0.001
60–70	55/101 (54)	2.44 (1.85–3.24)	<0.001
<60	35/47 (74)	4.19 (2.97–5.92)	<0.001
TLC (%) (n = 1904)			
>80	475/1644 (29)	Referent	
70–80	86/187 (46)	1.87 (1.49–2.36)	<0.001
60–70	33/56 (59)	2.64 (1.85–3.76)	<0.001
<60	13/17 (76)	4.35 (2.51–7.55)	<0.001
DLCO (%) (n = 1893)			
>80	245/995 (25)	Referent	
70–80	127/408 (31)	1.28 (1.03–1.59)	0.023
60–70	142/311 (46)	2.12 (1.72–2.60)	<0.001
<60	91/179 (51)	2.50 (1.96–3.18)	<0.001
LFS category (n = 1893)			
0 (LFS 2)	205/849 (24)	Referent	
1 (LFS 3–5)	291/851 (34)	1.50 (1.25–1.79)	<0.001
2 (LFS 6–9)	96/178 (54)	2.86 (2.25–3.65)	<0.001
3 (LFS 10–12)	13/15 (87)	5.64 (3.22–9.88)	<0.001

Definition of abbreviations: CI = confidence interval; LFS = Lung function score. Data was not available for all lung function parameters for all patients.

LEUKEMIA

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A SINGLE DOSE OF GEMTUZUMAB-OZOGAMICIN (GO) IN CONSOLIDATION PRIOR TO AUTOLOGOUS TRANSPLANT FOR YOUNGER PATIENTS WITH NEWLY DIAGNOSED ACUTE MYELOID (AML) IS SAFE BUT HAS NO EFFECT ON DISEASE FREE SURVIVAL: INTERIM RESULTS OF EASTERN COOPERATIVE ONCOLOGY GROUP STUDY (E1900)

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